PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RS101	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IB2004/051833	International filing date *(day/month/year)* 23.09.2004	Priority date *(day/month/year)* 28.09.2003
International Patent Classification (IPC) or national classification and IPC A61L31/02, A61L31/14		
Applicant SCHNYDER, Guido		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 10 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11.04.2005	19.09.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Heck, G Telephone No. +31 70 340-3288

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/051833

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
2-4, 7, 9-11, 13	as originally filed
1, 5, 6, 8, 12, 12a	received on 15.04.2005 with letter of 11.04.2005
Claims, Numbers	
1-20	received on 15.04.2005 with letter of 11.04.2005
Drawings, Sheets	
1/1	received on 15.04.2005 with letter of 11.04.2005

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-20
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement under Article 35(2) PCT with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents (D1-D4):

D1 ... US 4,602,632 A (Jorgensen R.)
D2 ... WO 02/053202 A (Hausdorf G. et al.)
D3 ... US 2002/004060 A (Heublein B. et al.)
D4 ... US 6,506,210 A (Kanner G.)

Document D1 discloses (cf. col. 3, par. 4 ; claim 1) a bioabsorbable metal hemostatic clip for occluding blood vessels during surgical procedures.
Document D2 discloses (cf. claims 1-3) biodegradable medical implants such as stents or surgical clips made of a metallic alloy based on tungsten, rhenium, osmium or molybdenum.
Document D3 discloses (cf. claims 1-7, 18) a medical implant in form of a coil, an umbrella, a stent, a wire network, a clip or a plug made of a biodegradable metallic material containing magnesium, iron or zinc as main constituent.
Document D4 discloses (cf. col. 1, l. 7-22 ; claim 1) a tissue stapler comprising a plurality of prongs for closing puncture wounds.

The subject-matter of claims 1-20 of the present application differs from D1-D3 in that the member is suitable for urging together portions of tissue resulting from a puncture wound and from D4 in the choice of bioresorbable and/or biodegradable material and is therefore novel according to Article 33(2) PCT.

Document D4, which is considered the most relevant state of the art, discloses (cf. col. 1, l. 7-22 ; claim 1) a tissue stapler comprising a plurality of prongs for closing puncture wounds.

In view of D4, the objective technical problem underlying the present application can be formulated as to reduce the risk of injuries or other complications following application of

sealing members for urging together two or more portions of body tissue from a puncture wound.

The solution is a sealing member made of a material selected from metals, alloys and ceramic compounds thereof, said material being bioresorbable and/or biodegradable.

Since the sealing member according to the present application is present in the body for a limited time, the risk of subsequent injury by external compression of the sealing member in the body is greatly reduced.

Biodegradable and bioabsorbable metallic materials have been used in the prior art for making surgical devices. However, the skilled person had no suggestion or incentive to modify the metallic or ceramic materials used in D4 to make them bioresorbable and/or biodegradable. Consequently, the subject-matter of claims 1-20 of the present application is considered to involve an inventive step according to Article 33(3) PCT.

MEMBER FOR VASCULAR SEALING

Field of the invention

The present invention relates to closing apertures in body tissues caused by punctures. More specifically, the present invention relates to sealing members such as a staple, snap or rivet for scarring such apertures.

Background

It frequently happens that portions of internal body tissue need to be sealed together. Often this need is a result of a cardiac or peripheral vascular catheterization. The art of sealing body tissues will therefore be discussed with a particular emphasis on closing apertures resulting of such interventions. Cardiac or peripheral vascular catheterizations are well known procedures that typically involve the making of a puncture in the femoral, radial or brachial artery to allow catheter insertions for diagnosis or treatment of cardiovascular or peripheral vascular diseases. After diagnostic and/or interventional catheterizations, the puncture formed by the insertion of the catheter must be closed following removal of the catheter. The puncture opening in the artery has a typical size in the range of 4-6 French for diagnostic procedures and in the range of 6-15 French for interventional procedures. Traditionally, manual or mechanical compressions are applied to puncture sites for at least 20 minutes and up to 6 hours after removal of the catheter. Other traditional methods for sealing the puncture site include the use of thrombotic or collagen plugs, patches, or other suturing methods.

The anatomy and in particular the length of the common femoral artery have been quantified to allow optimal puncture thereof. It has been found that the ideal puncture site is located in the area overlapping the upper inner quadrant of the femoral head, as it accurately predicts access in the common femoral artery whose length ranges from 0 to 11cm (mean: 6.7cm). This limits the remaining accessible segment of the common femoral artery to a length of about 2.0cm (Schnyder, G. et al., in Catheterization and Cardiovascular Interventions, vol. 53, pp. 289-295 [2001]). Since the staple described in U.S. Pat. No. 6,506,210 has a diameter of 3-4mm when fully expanded during implantation, it follows that such a staple can only be used a limited number of times (two to three) at the same location. This is problematic for treating patients with extensive vascular disease, who require a plurality of interventions.

Summary of the invention

It is an object of the present invention to reduce the risk of injuries or other complications following application of the above described prior art sealing members. The present invention relates to a member for urging together two or more portions of body tissue that form a wound caused by a puncture, in particular a puncture resulting from a catheter-based intervention, and maintaining these portions together until they are secured together by scarring thereof. According to the invention, the member is made of a material selected from at least one of metals, alloys and ceramic compounds thereof such as oxides, which material is bioresorbable and/or biodegradable.

The above portions of body tissue may forms a wound, such as a puncture resulting from a catheter-based intervention. However, in the context of the present invention, any puncture is contemplated, accidental or intentional.

The sealing member of the present invention can be used in and around the femoral, radial, and brachial arteries after coronary, cardiac or peripheral vascular procedures. The sealing member can be a staple, snap or rivet.

A bioresorbable material is a material that is transformed, when present in a body tissue, into smaller elements - such as colloidal particles - with the newly formed elements remaining in the body as traceable elements containing for example titanium, zirconium, niobium oxide, tantalum, silicon and lithium or compounds thereof.

A biodegradable material is a material that is transformed, when present in body tissue, into smaller elements - such as soluble salts - with the newly formed elements either remaining in the surrounding tissue as fine undetectable precipitates or dissolving and being ultimately eliminated from the body. These elements include for example magnesium, zinc, sodium, potassium, calcium, iron and manganese salts or compounds thereof.

The sealing member is advantageously made of materials which can undergo adequate plastic deformation (to enable insertion of the member with negligible elastic recoil) and strong mechanical properties so as to secure the wound site despite shear forces generated by blood flow within the vessel and by the surrounding tissue when the patient is moving (i.e. walking, climbing stairs, etc...).

It will be appreciated throughout the following description that the members of the present invention are made of any bioresorbable and/or biodegradable material that fulfills the above required properties of deformability and mechanical resistance.

Such materials have previously been used to manufacture vessel wall supports or stents, as described in U.S. Pat. No. 6,287,332 (assigned to Biotronik Mess- und Therapiegeraete GmbH & Co.), the disclosure of which is hereby incorporated by way of reference. Such stents are used to minimize inflammatory reaction so as to reduce the production of scar material upon implantation, whereby instent restenosis or renarrowing of the previously treated vessel segment by scar material is prevented. Surprisingly, sealing members made of these bioresorbable and/or biodegradable materials according to the invention do not prevent secure scarring but permit adequate healing.

The material of the member can be made of a combination of metals which can dissolve in the body without significantly forming bio-incompatible decomposition products. The material may dissolve at a rate in the range from 0.1 to 5 mg/day, in particular from 0.5 to 2mg/day. A sealing member made of this material may be

particular one of the suitable titanium alloys containing one of lithium, sodium, potassium, manganese calcium and iron, as explained above.

The invention will be further explained in the following Exemples:

Example 1

A bioresorbable and/or biodegradable sealing member according to the invention can be made from an alloy containing zinc as the component A and calcium as the component B. The weight ratio that zinc bears to calcium amounts to 25/1. This Zn-Ca alloy forms soluble salts as degradation products, such as calcium hydroxide which possesses such a high solubility that the solubility product is not transgressed during slow decomposition over several weeks or months. This hydroxide is transported in dissolved form by interstitial fluids or blood and is metabolized.

To improve the mechanical properties of the sealing member, such as ductility, hardness and tensile strength, suitable alloy constituents can be added in low concentrations. For instance, phosphorus may be added to the alloy in an amount of the order of a few percents.

Example 2

A bioresorbable and/or biodegradable metal sealing member acting as a local electrochemical device according to the invention can comprise a support body and a local

leads to active degradation of the sealing member. The degradation rate and thus the decomposition rate of the sealing member can be controlled by the size of the local electrode and by the selection of the metals of the sealing member.

Brief Description of the Drawings

The appended Figures show comparative staples as disclosed in the abovementioned US 6,506,210, wherein: Fig. 1 shows a staple; and Fig. 2 shows a staple which is being deployed with the aid of a stapler into tissue.

Detailed description

Fig. 1 shows a comparative staple 50 with a plurality of prongs 52 that can be deployed into tissue around a wound site to close a wound in a vessel wall caused by a puncture formed during catheterization. Fig. 2 shows staple 50 after having been deployed with the aid of a stapler into tissue to close a wound. During stapling, prongs 52 can be first extended outwardly so as to grasp large portions of tissue around the wound, and so that insertion of prongs 52 into the tissue occurs away from the wound, thereby providing a more consistent wound closure. Staples and process for inserting them into tissue around a wound is explained in greater detail in US 6,506,210.

This prior art staple 50 is made of biocompatible and/or bioabsorbable materials, including for example titanium, (and titanium alloys) stainless steel, polymeric materials (synthetic and/or natural), ceramic, etc. As opposed to the members, in particular staples, of the present invention, this prior art staple is not made of a bioresorbable and/or biodegradable material, in

CLAIMS

1. A member, such as a staple or rivet, for urging together two or more portions of tissue of a body which tissue portions form a wound caused by a puncture, in particular a puncture resulting from a catheter-based intervention, and maintaining said portions together until said portions are secured together by scarring thereof, wherein said member is made of a material selected from at least one of metals, alloys and ceramic compounds thereof, such as oxides, said material being:

- a bioresorbable material which is transformable in said tissue into smaller elements, such as colloidal particles, that remain in said body as traceable elements; and/or
- a biodegradable material which is transformable in said tissue into smaller elements, such as soluble salts, that remain in surrounding tissue as fine undetectable precipitates or that dissolve and are ultimately eliminated from said body.

2. The member of claim 1, wherein said material is a metal alloy containing: a first component which covers itself with a protective oxide coat; and a second component which ensure sufficient dissolution of the oxide coat.

3. The member of claim 2, wherein the first component comprises at least one metal selected from magnesium, titanium, zirconium, niobium, tantalum, zinc and silicon and the second component comprises at least one metal selected from lithium, sodium, potassium, manganese calcium and iron.

4. The member of claim 2 or 3, wherein the components of the metal alloy are selected such that corrosion products originate therefrom in the form of soluble salts, fine particles or colloidal particles or a mixture thereof.

5. The member of claim 2, 3 or 4, wherein the alloy contains zinc as a corrosion-inhibiting component.

6. The member of claim 5, wherein the alloy contains zinc and calcium.

7. The member of claim 6, wherein the alloy has a zinc/calcium weight ratio of at least 21/1.

8. The member of claim 2, 3, or 4, wherein the alloy contains sodium and magnesium.

9. The member of claim 1, wherein the bioresorbable and/or biodegradable material is an alloy of zinc and titanium.

10. The member of claim 9, wherein the zinc-titanium alloy has a weight percentage of titanium of 0.1% to 1%.

11. The member of claim 10, wherein an amount of 0.1 to 2 weight% gold is added as a further component to the zinc titanium alloy.

12. The member of claim 1, wherein the bioresorbable and/or biodegradable sealing member comprises a support body made of a substantially pure first metal and a local electrode made of a second metal which is in contact with the support body to produce a contact voltage and a resulting current that leads to active degradation of the sealing member.

13. The member of claim 12, wherein the local electrode is a coat on the support body.

14. The member of claim 12, wherein the local electrode is a metal part attached to the support body.

15. The member of claim 12, 13 or 14 wherein the support body consists essentially of zinc.

16. The member of claim 12, 13 or 14 wherein the local electrode consists essentially of a precious metal.

17. The member of claim 13, wherein said coat is deposited by electroplating or sputtering.

18. The member of any preceding claim, wherein the sealing member is made of a phosphorus-containing alloy.

19. The member of any preceding claim, which is a hydrogen-treated alloy.

20. The member of any preceding claim, which is made of an alloy which during use corrodes at such a rate that gases arising during corrosion physically dissolves in a body fluid to which the alloy is exposed.

FIG. 1

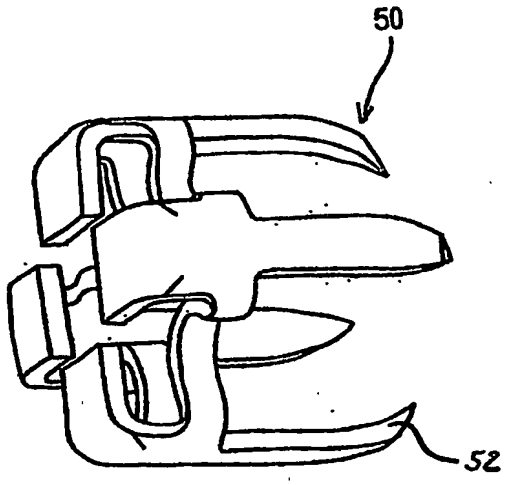

FIG. 2